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(54) Title: LOW-SODIUM LAXATIVE AND LAVAGE FORMULATION

(57) Abstract

A solution for use in the treatment of constipation and to produce cleansing of the colon. The solution for use in treating constipation can be comprised of polyethylene glycol or of polyethylene glycol and sodium ions, potassium ions, chloride ions and bicarbonate ions. The solution for use in producing cleansing of the colon is comprised of polyethylene glycol, sodium ions, potassium ions, chloride ions and bicarbonate ions; the ions are present in the solution in sufficient amounts to prevent net loss or gain of electrolytes from the body. A method of treating constipation and a method of effecting cleansing of the colon are also disclosed.

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LOW-SODIUM LAXATIVE AND LAVAGE FORMULATION

Technical Field

This invention is in the field of medicine and in particular relates to the treatment of constipation and to colon cleansing necessary, for example, prior to diagnostic procedures or surgery.

Background Art

Constipation is a common and often serious problem for which numerous treatments have been developed. None of these, however, has proved to be entirely successful and many have serious limitations. For example, dietary manipulations (e.g., increasing the fiber content of the diet, removing foods thought to have a constipating effect), laxatives and enemas are three commonly used approaches to solving the problem. However, these approaches have important limitations, such as their ability to produce the desired effect; user acceptance and compliance; and gas production (e.g., as a result of metabolism of fiber or carbohydrates, such as lactulose, by intestinal bacteria). In addition, ingestion of laxatives can cause damage to the surface of the intestinal mucosa; ingestion of large quantities can cause loss of body water and electrolytes (particularly potassium ions) and possibly kidney failure.

Colon cleansing is very important prior to a number of diagnostic or surgical procedures. For example, thorough cleansing of the colon is said to be "essential to a successful diagnostic barium enema" and "one of the most important steps in the diagnosis of early colon cancer." Davis, G.R. and H.R. Smith, Gastrointestinal Radiology, 8: 173-176 (1983). Colon cleansing is also necessary before colonscopy or colon surgery.

A variety of methods can be used for colon cleansing; each, however, has important shortcomings and none is wholly successful. Dietary manipulation, laxatives and enemas are traditionally used for colon cleansing. For example, Thomas and co-workers have shown that clear liquids for 48 hours, in combination with laxatives and enemas, are relatively successful in producing a feces-free colon. Thomas, G. et al., Gastroenterology, 82: 435-437 (1982). These approaches are time consuming, inconvenient and unpleasant for the patient. Potentially harmful salt and water losses may occur when cathartics and enemas are used. Davis, G. et al., Gastroenterology, 78: 991-995 (1980).

Another approach to colon cleansing is intestinal lavage, in which a large volume of an electrolyte solution is ingested, either by drinking or infusion by tube. The main component of the solution has typically been sodium chloride. Its consumption results in volume-induced diarrhea and thus cleansing of the colon. This method is generally faster than the traditional approaches, but there are questions about both the efficacy and the

safety of lavage. A significant percentage of saline-based lavage solutions is absorbed by the user and a rapid increase in intravascular volume results. Consequently, this approach is unadvisable in individuals unable to excrete a water and salt load because of cardiac or renal disease. Thomas, G. et al., Gastroenterology, 82: 435-437 (1982); Goldman, J. and M. Reichelderfer, Gastrointestianl Endoscopy, 28: 9-11 (1982). Bacterial fermentation of mannitol, which is a component of some lavage solutions, may produce explosive gas mixtures in the colon.

In 1980, Davis and co-workers reported the development of a lavage solution described as associated with minimal water and electrolyte absorption or secretion. Davis, G.R. et al., Gastroenterology, 78: 991-995 (1980); Davis G.R. and H.R. Smith, Gastrointestinal Radiology, 8: 173-176 (1983). The basic and critical ingredient in the solution is sodium sulfate, which is poorly absorbed; sodium absorption is markedly reduced when sulfate, rather than chloride or bicarbonate, is the predominant intraluminal anion. In addition to the sodium sulfate, the solution described contains sodium chloride, potassium chloride, sodium bicarbonate, polyethylene glycol or mannitol and water. The resulting solution has been shown to be effective in cleansing the gastrointestinal tract but it has disadvantages which interfere with its use. For example, patient acceptance can be a problem because of the solution's flavor, which is highly salty.

There is a need for a method of treating constipation which is not only effective, but also acceptable. Although there are many methods which can be used for colon cleansing prior to diagnostic or surgical procedures, none is without limitations. Thus, there is also a need for a method of colon cleansing which is safe, more effective and better accepted by users than presently available methods.

Disclosure of the Invention

The present invention relates to a formulation for the treatment of constipation and for colon cleansing, as well as a method for its use in treating constipation and producing cleansing of the colon. The formulation is comprised of polyethylene glycol (PEG), which, in the treatment of constipation, can be administered alone in an aqueous solution or can be administered in combination with electrolytes in an aqueous solution. In intestinal lavage, PEG is administered in combination with electrolytes in an aqueous solution. In treating constipation, the polyethylene glycol solution is administered in sufficient quantities to produce a soft stool. In effecting cleansing of the colon, the polyethylene glycol-electrolyte solution is administered orally or nasogastrically in sufficient quantities to produce rapid and thorough evacuation of the gastrointestinal tract. If electrolytes are present in the solution, they occur in amounts that will prevent a net loss of electrolytes from the body as a result of consumption of the solution. The sodium concentration of the formulation of the

present invention is considerably lower than in the sodium-sulfate-based lavage solutions now in use. Therefore, the lavage solution does not have a salty taste, as do the sodium-sulfate-based solutions.

There are at least three important advantages to the use of PEG in the treatment of constipation. First, PEG is poorly absorbed or not absorbed at all in the gastrointestinal tract; in addition, it is not fermented by colonic bacteria; therefore, PEG is not metabolized to products which can be absorbed or to gaseous products (such as hydrogen gas) which can cause patient discomfort (e.g., flatulence). In contrast, mannitol, which is also poorly absorbed, is fermentable by colonic bacteria and some of the fermentation products are absorbed in the colon; some of the fermentation products are gases. Second, when PEG is used in the treatment of constipation, stool weight remains elevated, even after PEG is consumed for three consecutive days; this is apparently due to the fact that because PEG is not metabolized by colonic bacteria, there is no adaptive increase in the bacterial population with time. Third, consumption of PEG does not adversely affect the intestinal mucosa.

Similarly, the fact that PEG is poorly absorbed or not absorbed at all in the gastrointestinal tract and is not fermented by colonic bacteria is advantageous in its use as a lavage solution for colon cleansing. As a result, there is no rapid increase in intravascular volume and no production of potentially explosive gases.

Brief Description of the Drawing

The figure represents graphically the secretion and absorption of water and electrolytes after lavage with a balanced electrolyte solution (BES), Golytely (GL) or the low sodium-PEG lavage solution of the present invention.

Detailed Description of the Invention

PEG in sufficient quantity in an aqueous solution to produce a soft stool can be used for treatment of constipation. Similarly, PEG in an aqueous solution can be administered orally or nasogastrically to effectuate rapid evacuation of the gastrointestinal tract. In the treatment of constipation, PEG can be administered alone or in combination with electrolytes. In effecting colon cleansing, PEG is administered in combination with electrolytes. In the PEG-electrolyte formulations, electrolytes are present in sufficient quantities to prevent a net electrolyte loss from the body. Electrolytes included in a solution of the present invention include sodium ions, potassium ions chloride ions, and bicarbonate ions, alone or in any desired combination. The PEG solution of the PEG-electrolyte solution can also contain flavoring material, such as Crystal Light^{R}, aspartame or other suitable flavoring agent.

The sodium concentration of the formulation of this invention is less than 100 milliequivalents per liter, and will generally be less than 75 milliequivalents per liter. In one preferred embodiment, the sodium concentration is about 65 milliequivalents

per liter. This is much lower than the sodium concentration of the two sodium-sulfate based lavage solutions (Golytely and Colyte) currently available. (The sodium concentration of these two solutions is 125 milliequivalents per liter.) Because of its low sodium content, the solution of the present invention does not have the highly salty taste complained of by users of presently available solutions.

According to the present invention, from about 75 to about 300 grams of PEG is present in a liter of solution. In one preferred embodiment, PEG 3350 is present in water at a concentration of about 105 grams (gm) per liter of solution. Each of the ions is present in a concentration of from about 2 to about 100 milliequivalents. In one preferred embodiment, sodium ions are present in a concentration of about 65 milliequivalents per liter, chloride in a concentration of about 53 milliequivalents per liter, bicarbonate ions in a concentration of about 17 meq per liter and potassium ions in a concentration of about 5 meq per liter. .

In another preferred embodiment, PEG 3350 is present in water at a concentration of about 120 gm per liter of solution. In another embodiment, about 120 gm of PEG 3350 is present per liter of solution along with sodium ions, potassium ions, chloride ions and bicarbonate ions. Each of the ions is present in a concentration of from about 5.0 milliequivalents per liter to about 50 milliequivalents per liter; in a preferred embodiment, they are present in a liter of solution in the following concentrations: sodium ions, 46.6 milliequivalents;

potassium ions, 9.0 milliequivalents; chloride ions, 35.0 milliequivalents; and bicarbonate ions, 20.9 milliequivalents.

The PEG solution of this invention is made by combining PEG 3350 with sufficient water to make a liter of solution. For example, in one embodiment, about 105gm of PEG 3350 is combined with sufficient water to make a liter of solution. In another embodiment, about 120 gm. of PEG 3350 is combined with sufficient water to make a liter of solution. If the PEG solution is to contain electrolytes as well, sources of the ions listed above (in dry form) are combined with PEG and mixed in a standard blender. The PEG-electrolyte solution is made by combining the PEG-electrolyte mixture with enough water to make a liter of solution.

In the treatment of constipation, individuals consume from about 50 to about 500 milliliters of either the PEG solution or the PEG-electrolyte solution, generally once a day or with meals. In one preferred embodiment, individuals consume about 250 milliliters of either the PEG solution or the PEG-electrolyte solution. In particular, they consume about 250 milliliters of either the PEG solution having about 105 gm. of PEG 3350 in sufficient water to make a liter of solution or the PEG-electrolyte solution having the same PEG 3350 concentration. If the solution also has electrolytes, each is present in a concentration of from about 2 milliequivalents to about 100 milliequivalents per liter. Consumption of this quantity

should result in an increase in stool weight of from about 100 gm to about 300 gm. per day and thus relieve constipation.

Administration of this quantity of PEG will cause an increase in stool water, as well as produce a soft stool. These two changes will contribute to a solution to the problem of constipation. In addition, PEG is not fermented by colonic bacteria and there is no production of gases (such as hydrogen gas) which can cause flatus and associated discomfort in the user. There will be no significant loss of electrolytes from the body particularly when the electrolytes listed above are included in the PEG solution.

For colon cleansing, individuals are generally lavaged with the PEG-electrolyte solution at a rate of about 20-30 milliliters per minute (1.2-1.8 liters per hour). That is, the solution is administered orally or nasogastrically at this rate. In the PEG-electrolyte solution, the electrolytes are each present in a concentration of from about 2 milliequivalents to about 100 milliequivalents per liter. The total volume of solution necessary to produce colon cleansing varies from individual to individual; it generally will be from 3 to 4 liters, although some individuals will require smaller or larger quantities. In one embodiment, individuals are lavaged at the rate of 20 milliliters per minute with the PEG-electrolyte solution having about 120 gm. of PEG 3350, 1.68 grams sodium bicarbonate, 0.74 gm potassium chloride and 1.46 gm sodium chloride in sufficient water to make a liter of solution. In a second embodiment, they are lavaged with PEG-electro-

lyte solution have the following components, each expressed as grams/liter of solution: PEG 3350, 105; sodium chloride, 2.80; sodium bicarbonate, 1.43 and potassium chloride, 0.37.

This invention is further illustrated by the examples given below which are not to be seen as limiting in any way.

Example 1 Osmolality of Polyethylene Glycol Solutions

Polyethylene glycol (PEG) was dissolved in water in the amounts shown in Table 1. The osmolality of each solution was measured by freezing point depression. As shown in Table 1, as the concentration of PEG is increased, the osmolality increases disproportionately. For example, a solution containing 60gm PEG per liter is osmotically equivalent to 40mOsm/Kg. When the concentration of PEG is doubled, to 120gm per liter of solution, the osmolality increases almost fourfold (to 156MOsm/Kg.).

Table 1 Osmolality of PEG Solutions

PEG Concentration (gm/liter)	Osmolality (mOsm/Kg.)
50	35
60	40
100	103
120	156
150	255
200	475

Example 2 Effect of PEG Ingestion on Stool Weight and Comparison with the Effect of Mannitol Ingestion on Stool Weight

Four subjects consumed mannitol in an aqueous solution and eight subjects consumed PEG in an aqueous solution for three consecutive days. The amount of mannitol or PEG consumed by each subject is shown in Table 2; the PEG solutions consumed by the eight subjects contained approximately 60 grams of PEG per liter. Prior to treatment, the stool weight (gm./day) for each subject was determined. Stool weight was also determined for each of the three days during which subjects consumed either mannitol or PEG. These weights are also shown in Table 2.

TABLE 2

Quantity of Mannitol or PEG Consumed; Stool Weights

Subjects Consuming Mannitol	Amount Consumed (gms)	(mMoles)	Stool Weight (gm./24hr.) No Treatment	Treatment Days 1	2	3
1	17	96	175	380	424	271
2	17	96	133	356	417	179
3	17	96	147	515	494	146
4	26	144	195	656	515	205
MEAN±SEM[1]			162 ±14	477 ±69	462 25	200 26
Subjects Consuming PEG						
1	72	21	129	290	398	861
2	72	21	116	625	566	507
3	72	21	195	563	692	531
4	72	21	102	641	183	510
5	108	32	62	930	866	695
6	108	32	147	1442	1006	1056
7	144	43	175	1096	1274	942
8	144	43	133	1638	1097	1858
MEAN±SEM[1]			132 +15	903 ±114	760 ±131	870 ±154

[1]Standard error of the mean

Stool weights were greater than the pretreatment stool weights on day 1 and day 2 for those consuming mannitol; on day 3, however, for all four subjects, the stool weight was less than on the two previous days and in three of the four cases, approached the pretreatment weight. In contrast, stool weight remained greater on each of the three days for those consuming the PEG solution. This difference appears to be due to the fact that colonic bacteria can ferment the mannitol, but not the PEG. When a mannitol solution is consumed, there apparently is an adaptive increase in colonic bacteria during day one and day two, with the result that almost all of the mannitol is fermented and the laxative effect prevented after the initial period of administration. None of the subjects consuming PEG complained of excessive flatus; this was a troublesome symptom in those ingesting mannitol. This is also probably the result of the nonfermentable nature of PEG.

Example 3 Use of Low Sodium-PEG Solution to Produce Cleansing of the Colon

A normal subject was lavaged at the rate of 30 milliliters per minute (1.8 liters per hour) with a solution having the following composition:

PEG concentration	120	g/L of solution*
Measured Sodium conc	46.6	mEq/L of solution
Measured potassium conc	9.0	mEq/L of solution
Measured chloride conc	35.0	mEq/L of solution
Measured bicarbonate conc	20.9	mEq/L of solution
Osmolality	293	mOs/Kg of water

* Equivalent to 156 mOsm/Kg when present as the only solute.

The solution had been made by combining 120 gm. PEG; 1.68 gm. sodium bicarbonate ($NaHCO_3$); 0.74 gm. potassium chloride (KCl); and 1.46 gm. sodium chloride (NaCl) and adding sufficient water to make one liter of solution.

Results of colon cleansing with this solution were compared with results produced using a balanced electrolyte solution (BES) and Golytely (GL). They are best described with reference to the figure. Golytely is the tradename for the lavage solution, described by Davis and co-workers, which is based primarily on sodium sulfate (see above). The results with the low sodium-PEG solution of the present invention are indicated by an X, plotted in between results for the other two solutions.

These results show that use of the low sodium-PEG solution is associated with negligible body gains or losses of water, sodium, chloride, bicarbonate and potassium.

Example 4 Use of Low-Sodium-EPG Solution in a Perfusion Study

Study Design

After an overnight fast, subjects swallowed a single-lumen, mercury-weighted polyvinyl tube, the tip of which was in the stomach. A solution having the following components was used in the study:

Component	Concentration (gm/liter)
PEG 3350	105.00
Sodium chloride	2.80
Sodium bicarbonate	1.43
Potassium chloride	0.37

This solution had the following concentrations of active ingredients:

Component	Concentration (meq/liter)
Sodium	65
Chloride	53
Bicarbonate	17
Potassium	5

PEG-3350 was present in the solution in a concentration of 31.30 mmol/liter.

The solution was warmed to room temperature and infused into the stomach at a pump speed of 20 ml/minute or 30 ml/minute. The polyethylene present in the solution as an integral part of the formulation was also used as a nonabsorbable marker to assess water absorption or secretion (see below).

Twenty minutes after the start of the gastric infusion, the infusion of the solution was momentarily interrupted and 200 mg of sulfabromphthalein (BSP) was injected into the stomach through the polyvinyl tube. The infusion was then restarted at the same rate.

When all BSP has been eliminated, a steady state has been achieved. When such a state was achieved, a rectal tube was inserted into the rectum for collection of rectal effluent.

The perfusion was continued for two hours after steady state conditions were achieved. This two-hour period consisted of two 60 minute collection periods, during which PEG concentrations remained essentially the same, showing that a "steady state" existed. The collected samples of rectal effluent were then analyzed for PEG concentration, and electrolyte concentrations by standard methods. Net water and electrolyte movement were calculated by use of standard nonabsorbable marker equations (see below). The results obtained in this study were compared with results obtained when a second group of subjects was infused under similar conditions with a sodium sulfate-based solution which also contained small amounts of PEG, chloride, bicarbonate and potassium. This solution is commercially available under the name Golytely^{R}. Significance of differences between results was determined by group t-analysis.

Data and Calculations

Results of the perfusion studies are shown in Table 3 and Table 4.

In the tables, a(+) preceeding a value indicates net secretion and a(-) indicates net absorption

Table 3 Perfusion with Low-Sodium-PEG Solution

Subject	Infusion Rate	Water	Ions			
			Sodium	Potassium	Chloride	Bicarbonate
	(ml/min)	(ml/hr)	(meq/hr)	(meq/hr)	(meq/hr)	(meq/hr)
1	19.1	-223.0	-15.8	-1.1	-13.0	-0.2
2	20.3	-28.0	3.1	-0.3	8.0	1.4
3	20.1	-66.0	5.2	-0.6	10.4	0.2
4	21.4	-7.0	5.2	0.1	10.4	2.4
5	20.7	164.0	31.6	0.3	32.7	5.7
6	21.2	-93.0	-7.1	-1.8	-2.7	-1.6
7	20.8	-65.0	10.1	-0.6	23.4	0.8
8	30.9	130.0	27.6	0.9	36.0	6.4
9	29.8	-62.0	5.6	0.1	10.7	5.2
10	29.8	-228.0	-23.9	0.4	-12.0	-8.2
11	29.5	-107.0	-0.5	-0.8	10.7	-2.5
12	29.8	10.0	7.2	0.9	16.7	5.4
13	30.1	36.0	10.2	1.6	28.7	-1.5
14	30.1	-24.0	10.3	2.0	22.7	-6.0
mean		-40.2	4.9	0.07	13.1	0.5

Table 4 Perfusion with Sodium-Sulfate-Based Solution

Subject	Infusion Rate	Water	Ions			
			Sodium	Potassium	Chloride	Bicarbonate
	(ml/min)	(ml/hr)	(meq/hr)	(meq/hr)	(meq/hr)	(meq/hr)
1	30.8	-77.0	-4.1	-2.7	7.6	-15.2
2	29.0	-198.0	-27.4	-5.5	-5.8	-7.3
3	31.0	-33.0	-1.0	-2.4	-4.4	-6.7
4	29.2	-116.0	-18.8	-4.8	-14.7	-7.3
5	28.1	-7.0	-10.9	-2.9	-0.7	-8.3
6	30.5	163.0	24.9	7.4	34.3	-7.6
7	26.8	-30.0	-1.8	-2.2	1.4	-5.6
8	29.7	-47.0	-4.7	-1.7	3.6	-8.5
9	30.2	16.0	13.7	-0.5	22.6	-6.3
10	27.8	-127.0	-3.6	-3.4	14.1	-9.6
11	26.7	-214.0	-25.8	-2.3	1.9	-13.3
12	24.9	-142.0	-13.1	-4.8	4.5	-8.9
13	23.6	41.0	2.9	-1.3	-	-3.9
14	26.4	-116.0	-3.1	-0.5	22.6	-6.3
mean		-63.4	-5.2	-2.0	6.7	-8.2

The results of significance testing are shown in Table 5

Table 5 t Test for Comparing Independent Means

measurement	s^2	t_{26}	P
Water	11111	0.6	> 0.1
Sodium	145	2.2	< 0.05
Potassium	5.4	2.2	< 0.05
Chloride	207	1.2	> 0.1
Bicarbonate	363	5.4	< 0.001

* n = 27

Where s^2 is the pooled estimate of common variance.

Of the parameters measured, sodium, potassium and bicarbonate showed significnat differences between the two formulations. To determine whether this difference represents an improvement, the following null hypothesis was tested: there is no difference between results obtained when the low-sodium-PEG solution was given and zero absorption/ secretion. Results of this analysis are shown in Table 6.

Table 6 t Test

measurement	s	t_{13}	P
Water	110	1.4	> 0.1
Sodium	9.7	1.9	> 0.05
Potassium	1.1	0.2	> 0.1
Chloride	15.1	3.2	< 0.01
Bicarbonate	4.4	0.4	> 0.1

Where s is the sample standard deviation.

These results indicate that no significant difference was observed between the data obtained when the low-sodium-PEG solution was administered and zero net absorption/secretion for all of the parameters measured, except for chloride, which was not significantly different from the sodium sulfate-based solution (Golytely). For sodium, potassium and bicarbonate, there is a substantial improvement over results obtained when the sodium sulfate-based solution was administered.

Industrial Utility

This invention has industrial application in the treatment of constipation, which is a common and often serious medical problem, and in cleansing of the colon, which is necessary, for example, prior to diagnostic and surgical procedures.

Equivalents

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, many equivalents to the specific materials and components described specifically herein. Such equivalents are intended to be encompassed in the scope of the following claims.

CLAIMS

1. A solution comprising, per liter, the following components:
   a. from about 75 grams to about 300 grams of polyethlyene glycol;
   b. from about 2 milliequivalents to about 100 milliequivalents of sodium ions;
   c. from about 2 milliequivalents to about 100 milliequivalents of potassium ions;
   d. from about 2 milliequivalents to about 100 milliequivalents of chloride ions; and
   e. from about 2 milliequivalents to about 100 milliequivalents of bicarbonate ions.

2. A solution for treatment of constipation comprising an aqueous solution of polyethylene glycol, said polyethylene glycol being present in an effective constipation-relieving quantity.

3. A solution of Claim 2 additionally containing:
   a. sodium ions;
   b. potassium ions;
   c. chloride ions; and
   d. bicarbonate ions,

in sufficient quantities to prevent a net loss of electrolytes in the person to whom the solution is administered.

4. A solution of Claim 2 in which polyethylene glycol 3350 is present in a concentration of from about 75 grams to about 300 grams per liter.

5. A solution of Claim 4 additionally containing from about 2 to about 100 milliequivalents of each of the following ions:

a. sodium ions;
b. potassium ions;
c. chloride ions and
d. bicarbonate ions.

6. A solution for treatment of constipation, said solution containing per liter, the following components:

a. about 105 grams of polyethylene glycol 3350;
b. from about 2 milliequivalents to about 100 milliequivalents of sodium ions;
c. from about 2 milliequivalents to about 100 milliequivalents of potassium ions;
d. from about 2 milliequivalents to about 100 milliequivalents of chloride ions; and
e. from about 2 milliequivalents to about 100 milliequivalents of bicarbonate ions.

7. A solution for use in the treatment of constipation in a person, said sodium being comprised of polyethylene glycol 3350 in sufficient quantities to produce softening of the stools produced by the person to whom the solution is administered.

8. A solution of Claim 7, additionally comprising sufficient quantites of:

a. sodium ions:
b. potassium ions:
c. chloride ions; and
d. bicarbonate ions,

to prevent a net loss of electrolytes from the body of the person to whom the solution is administered.

9. A method of treating constipation, comprising administering to a person sufficient quantities of a solution of polyethylene glycol to cause softening of the stools produced by the person to whom the solution is administered.

10. A method of Claim 9 wherein the solution additionally contains sufficient quantities of:

a. sodium ions;
b. potassium ions;
c. chloride ions; and
d. bicarbonate ions

to prevent a net loss of electrolytes from the body of the person to whom the solution is administered.

11. A method of treating constipation comprising administering to a person sufficient quantities of a solution to produce a laxative effect in the person, the solution comprising polyethylene glycol 3350.

12. A method of Claim 11 in which from about 50 to 500 milliliters of the solution is administered.

13. A method of Claim 12 in which a liter of the solution additionally contains from about 2 to about 100 milliequivalents of each of the following:

a. sodium ions;
b. potassium ions;
c. chloride ions; and
d. bicarbonate ions.

14. A method of treating constipation, comprising administering to a person sufficient quantities of a solution comprised of:

a. polyethylene glycol 3350;
b. sodium ions;
c. potassium ions;
d. chloride ions; and
e. bicarbonate ions,

to produce a laxative effect in the person, the concentrations of the ions in said solution sufficient to prevent a net loss of the ions from the body of the person to whom the solution is administered.

15. A solution which, administered orally or nasogastrically to a person, causes evacuation of the gastrointestinal tract, the solution being comprised of:

a. polyethylene glycol 3350;
b. sodium ions;
c. potassium ions;
d. chloride ions; and
e. bicarbonate ions.

16. A solution which will cause rapid cleansing of the gastrointestinal tract when administered orally or nasogastrically in sufficient quantities to a person, a liter of the solution comprising:

a. from about 75 grams to about 300 grams of polyethylene glycol;
b. from about 40 milliequivalents to about 70 milliequivalents of sodium ions;
c. from about 2 milliequivalents to about 15 milliequivalents of potassium ions;
d. from about 30 milliequivalents to about 60 milliequivalents of chloride ions; and
e. from about 10 milliequivalents to about 25 milliequivalents of bicarbonate ions.

17. A solution for causing evacuation of the colon, a liter of the solution being comprised of the following components:

    a. about 120 grams of polyethylene glycol 3350;
    b. about 46 milliequivalents of sodium ions.
    c. about 9 milliequivalents of potassium ions;
    d. about 35 milliequivalents of chloride ions; and
    e. about 21 milliequivalents of bicarbonate ions.

18. A solution for causing evacuation of the colon, a liter of the solution being comprised of the following components:

    a. about 105 grams of polyethylene glycol 3350;
    b. about 65 milliequivalents of sodium ions.
    c. about 5 milliequivalents of potassium ions;
    d. about 53 milliequivalents of chloride ions; and
    e. about 17 milliequivalents of bicarbonate ions.

19. A low-sodium lavage solution which, when administered to a person, will cause cleansing of the gastrointestinal tract, the solution having the following components: polyethylene glycol 3350, sodium ions, bicarbonate ions, these components being present in the solution in sufficient quantities to cause cleansing of the gastrointestinal tract.

20. A solution of Claim 19, a liter of the solution comprising:

a. about 105 grams of polyethylene glycol 3350;

b. about 65 milliequivalents of sodium ions;

c. about 5 milliequivalents of potassium ions;

d. about 53 milliequivalents of chloride ions; and

e. about 17 milliequivalents of bicarbonate ions.

21. A lavage solution having no added sulfate, which, when administered orally or nasogastrically in sufficient quantities to a person, causes cleansing of the gastrointestinal tract, the solution being comprised of polyethylene glycol 3350, sodium ions, potassium ions, chloride ions and bicarbonate ions, the concentrations of the ions being sufficient to prevent net absorption or excretion of those ions in the gastrointestinal tract.

22. In a solution, comprising electrolytes and polytheylene glycol 3350, which is administered to a person to cause cleansing of the gastro-intestinal tract, the improvement comprising a low sodium concentration and the absence of added sulfate.

23. A method of causing evacuation of the colon, comprising the administration of sufficient quantities of a solution to cause the evacuation, each liter of the solution comprising:

a. from about 75 grams to about 300 grams of polyethylene glycol;

b. from about 40 milliequivalents to about 70 milliequivalents of sodium ions;

c. from about 2 milliequivalents to about 15 milliequivalents of potassium ions;

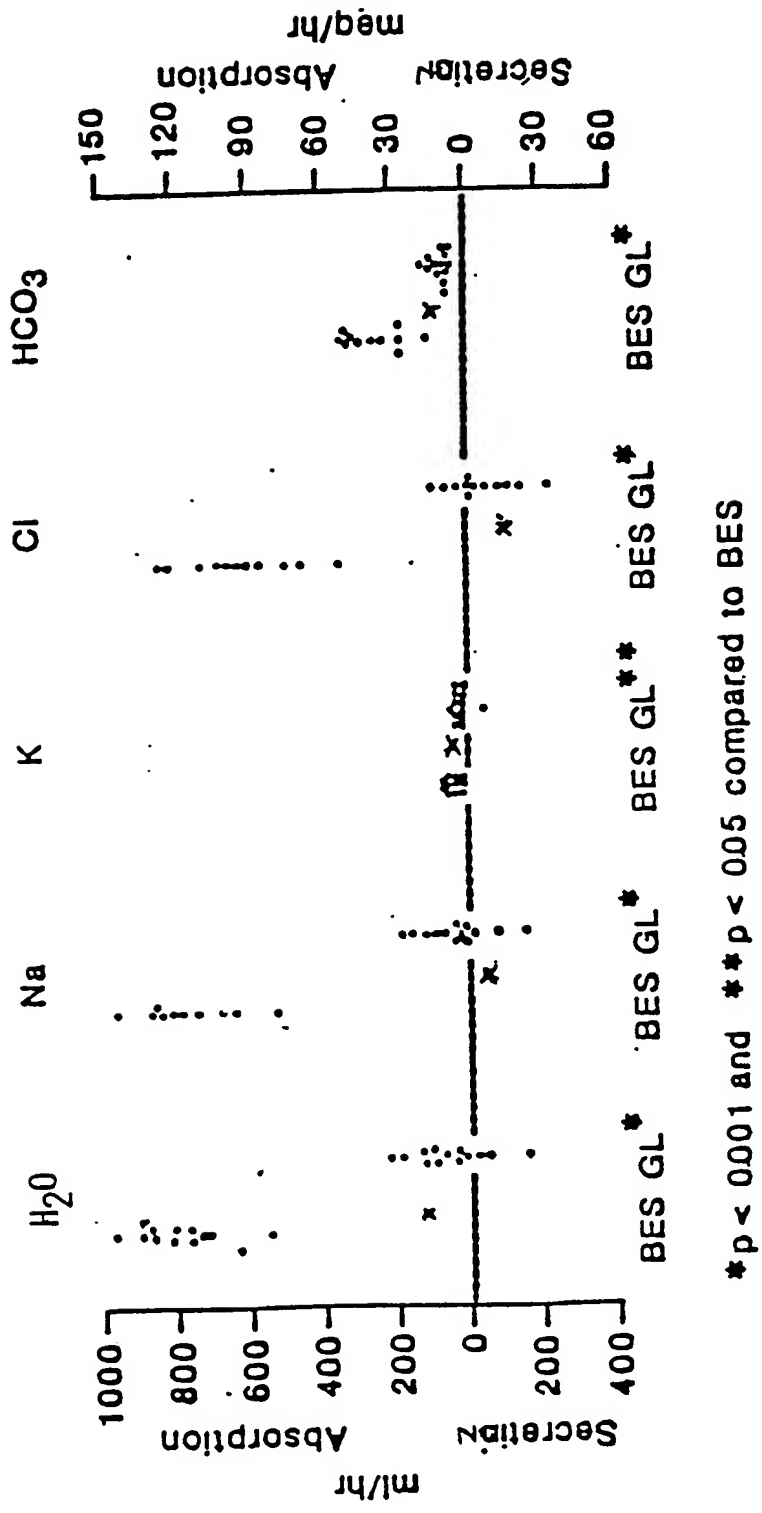
d. from about 30 milliequivalents to about 60 milliequivalents of chloride ions; and

e. from about 10 milliequivalents to about 25 milliequivalents of bicarbonate ions.

24. A method of cleansing the colon, comprising the administration of sufficient quantities of a solution to cause the cleansing, a liter of the solution comprising:

a. about 105 grams of polyethylene glycol;
b. about 65 milliequivalents of sodium ions;
c. about 5 milliequivalents of potassium ions;
d. about 53 milliequivalents of chloride ions; and
e. about 17 milliequivalents of bicarbonate ions.

25. In a method of causing the evacuation of the colon by oral or nasogastric administration of a lavage solution comprising electrolytes and polythylene glycol, the improvement comprising a lavage solution having a low sodium concentration and the absence of added sulfate.


mEq/hr
Absorption
Secretion
150
120
90
60
30
0
30
60
HCO_3
Cl
K
Na
H_2O
BES GL*
BES GL*
BES GL**
BES GL*
BES GL*
ml/hr
Absorption
Secretion
1000
800
600
400
200
0
200
400
*p < 0.001 and **p < 0.05 compared to BES

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 86/01578

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[4]: A 61 K 31/765; A 61 K 33/14; // (A 61 K 33/14, 33:00; 31:765)

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[4]	A 61 K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	US, A, 3495010 (SPENCER M. FOSSEL) 10 February 1970 see column 1, lines 45-53; column 3, lines 11-18	2,4,7
A	Unlisted Drugs, volume 37, no. 3, March 1985, (Chatham, New Jersey, US), see page 48-i "Colyte" (cited in the application)	1-8,15-22
A	Unlisted Drugs, volume 36, no. 8, August 1984, (Chatham, New Jersey, US), see page 153-1, "Golytely" (cited in the application)	1-8,15-22
A	Unlisted Drugs, volume 25, no. 3, March 1973 (Chatham, New Jersey, US), see page 39-e, "Alevac"	1-8,15-22

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
10th November 1986	16 DEC 1986
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	L. ROSSI

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. [X] OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This International search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. [X] Claim numbers °) ..... because they relate to subject matter not required to be searched by this Authority, namely:

°) Claims 9-14,23-25
See Rule 39.1.iv of PCT
Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods

2. [ ] Claim numbers ....., because they relate to parts of the International application that do not comply with the prescribed requirements to such an extent that no meaningful International search can be carried out, specifically:

3. [ ] Claim numbers ....., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. [ ] OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International search report covers all searchable claims of the International application.

2. [ ] As only some of the required additional search fees were timely paid by the applicant, this International search report covers only those claims of the International application for which fees were paid, specifically claims:

3. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. [ ] As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

[ ] The additional search fees were accompanied by applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON

INTERNATIONAL APPLICATION NO. PCT/US 86/01578 (SA 14222)

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 24/11/86

The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 3495010	10/02/70	None	